A look to future - ways to a complete scarless regeneration after severe skintrauma

The treatment of soft tissue injuries is the dominating operative procedure curing soldiers wounded in action. Frequently, the initial injury and/or further surgical treatment leave huge soft tissue defects which need to be reconstructed due to functional and aesthetic reasons. Additionally, the mainly young and prior to the trauma active patients have high expectations concerning their outcome. Although reconstructive possibilities and skills in central Europe and northern America are consistently impressive, the mostly severe and multiple wounded soldiers often stretch the caring surgeon to his limits. While tissue defects and their reconstruction are a relevant task especially in the acute and post-acute phase of rehabilitation, functional restrictions and psychological burden because of scar formation are medium- to long-term problems which must be avoided as good as possible.
Modern science might offer great options for the treatment of different types of defects in future, e.g. the use of stem cell supported or based therapies in severe injuries of the skin. Options for reducing or avoiding scar formation might come along with these attempts.

It is well known that proper activation of macrophages in the inflammatory phase of acute wound healing is essential for physiologic tissue repair. While fetal wound healing is able to proceed without scars, massive macrophage inflammatory responses may be causal for the fibrotic response always accompanying adult wound healing. The presented study addressed the question whether mesenchymal stem cells (MSCs) – due to their anti-inflammatory properties – represent a strategy to control macrophage activation and scar formation in a murine model of full-thickness skin wounds.
When MSCs were injected into wound margins we observed a significantly accelerated wound closure as well as a histologically reduced scar formation in contrast to the control group (injection of phosphate-buffered saline (PBS)).
We were able to show that the TNF-α stimulated protein 6 (TSG-6), which is released by MSCs, following injection into wound margins, suppressed the release of TNF-α from activated macrophages. This is of major importance because TNF-α leads to an enhancement of the inflammatory response causing impaired wound healing and most likely the extend of scar formation. Furthermore, our results showed that the injection of MSCs or recombinant TSG-6 lead to a suppression of myofibroblast differentiation which eventually is responsible for the characteristic tissue organization of scars in adult wound healing. Following this perception, we were able to show that injecting MSCs in acute wounds leads to a significantly reduced scar depth and a better scar texture compared to PBS-injected control wounds.
This study provides insight into what we believe to be a previously undescribed multifaceted role of MSCs-released TSG-6 in wound healing. MSCs-released TSG-6 was identified to improve wound healing by limiting macrophages activation, inflammation and fibrosis. TSG-6 and MSCs-based therapies may thus qualify as promising strategies to enhance tissue repair and to prevent excessive scar formation.

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